WO 2005/095377 PCT/GB2005/001200

1. A process for the preparation of a compound of formula (I):

wherein R¹ is C₁₋₆ alkyl; R² and R³ are, independently, C₁₋₆ alkyl; and R⁴ is C₁₋₆ alkyl or benzyl (wherein the phenyl ring of benzyl is optionally substituted by nitro, S(O)₂(C₁₋₄ alkyl), cyano, C₁₋₄ alkyl, C₁₋₄ alkoxy, C(O)(C₁₋₄ alkyl), N(C₁₋₆ alkyl)₂, CF₃ or OCF₃); the process comprising reacting a compound of formula (II):

$$\begin{array}{c}
HO \longrightarrow N \\
N \longrightarrow O \\
O \longrightarrow O \\
R^2 \times R^3
\end{array}$$
(II)

- wherein R², R³ and R⁴ are as defined above, with a suitable base; and reacting the product so formed with R¹OC(O)CH₂X, wherein R¹ is as defined above and X is chloro, bromo or iodo; wherein the process is carried out in a suitable solvent at a temperature in the range -40°C to -5°C; and wherein at least 0.2 moles of the compound of formula (II) are used in the process.
- 2. A process as claimed in claim 1 wherein R¹, R² and R³ are independently selected from C₁₋₄ alkyl.
 - 3. A process as claimed in claim 1 or 2 wherein R¹ is ethyl.

20

- 4. A process as claimed in claim 1, 2 or 3 wherein R^2 and R^3 are methyl.
- 5. A process as claimed in claim 1, 2, 3 or 4 wherein R^4 is benzyl optionally substituted by C_{1-4} alkyl.
- 6. A process as claimed in claim 1, 2, 3, 4 or 5 wherein R⁴ is unsubstituted benzyl.
- 7. A process as claimed in any one of claims 1 to 6 wherein X is bromo.
- 8. A process as claimed in any one of claims 1 to 7 wherein the base is an alkyl metal C₁₋₆ alkoxide.
- 9. A process as claimed in any one of claims 1 to 8 wherein the base is potassium tertbutoxide.

WO 2005/095377 PCT/GB2005/001200

6

- 10. A process as claimed in any one of claims 1 to 9 wherein the molar ratio of suitable base: R¹O₂CCH₂X: compound of formula (II) is (1 to 1.3):(1 to 1.3):1.
- 11. A process as claimed in any one of claims 1 to 10 wherein the molar ratio of suitable base: R¹O₂CCH₂X: compound of formula (II) is (1.1 to 1.3):(1.1 to 1.3):1.
- 12. A process as claimed in any one of claims 1 to 11 wherein the molar ratio of suitable base: R¹O₂CCH₂X: compound of formula (II) is 1.2:1.2:1.
- 13. A process as claimed in any one of claims 1 to 12 wherein the solvent is selected from a cyclic ether, an aliphatic ethers and an aromatic solvent.
- 14. A process as claimed in any one of claims 1 to 13 wherein the solvent is selected from tetrahydrofuran, diethyl ether, diisopropyl ether, methyl tert-butyl ether, benzene, toluene and xylene; and a mixture of two or more of said solvents.
- 15. A process as claimed in any one of claims 1 to 14 wherein the solvent is tetrahydrofuran.
- 16. A process as claimed in any one of claims 1 to 15 wherein the temperature is in the range -30°C to -10°C.
- 17. A process as claimed in any one of claims 1 to 16 wherein the temperature is in the range -25°C to -15°C.

20

5

10

15

25